

DR SATOSHI GANDO (Orcid ID : 0000-0002-3525-0750)

Article type : Letter to the Editor

DOACs and 'newer' haemophilia therapies in COVID-19

Jecko Thachil ¹

Ning Tang ²

Satoshi Gando ³

Anna Falanga ⁴

Marco Cattaneo ⁵

Marcel Levi ⁶

Cary Clark ⁷

Toshiaki Iba ⁸

Affiliations: ¹ Department of Haematology, Manchester University Hospitals, Oxford road, Manchester, United Kingdom, ² Tongji hospital, Huazhong University of Science and Technology, Wuhan, Hubei, China, ³ Department of Acute and Critical Care Medicine, Sapporo Higashi Tokushukai Hospital, Sapporo, Japan, ⁴ University of Milan Bicocca, Dept of Medicine and Surgery; Hospital Papa Giovanni, XXIII, Bergamo; Italy, ⁵ ASST Santi Paolo e Carlo, Dipartimento di Scienze della Salute, Università degli Studi di Milano, Milan. ITALY, ⁶ Department of Medicine and Cardio-metabolic Programme-NIHR UCLH/UCL BRC, University College London Hospitals NHS Foundation Trust, London, United Kingdom, ⁷ Director of Programs and Education, International Society on Thrombosis and Haemostasis ⁸ Department of Emergency and Disaster Medicine, Juntendo University Graduate School of Medicine, Tokyo, Japan.

Author for correspondence: Dr Jecko Thachil, Department of Haematology, Manchester Royal Infirmary, Oxford road, Manchester, United Kingdom. M13 9WL.

Phone: 0044 161 276 6448

Fax: 0044 161 276 8085

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/JTH.14841](#)

This article is protected by copyright. All rights reserved

Email: jecko.thachil@mft.nhs.uk

Conflicts of interests: None declared

Author contributions: JT and MC drafted the response; All the authors agreed and approved the final manuscript

Dear Editor,

We would like to thank the authors for their insightful thoughts on the consideration of anticoagulants and treatment for haemophilia A and B during the COVID-19 pandemic. They highlight some important practical points which certainly should be adopted by the thrombosis and haemostasis community in the current situation of restricted mobility, which reduces the possibility for patients to access general practitioners and hospitals. In relation to the use of direct oral anticoagulants (DOACs), the authors suggest to consider the current crisis as an opportunity to switch patients receiving vitamin K antagonists (VKA) to a DOAC as long as it is within the indication (excluding patients with mechanical heart valves or antiphospholipid syndrome). In addition, we think this may be an opportunity to consider DOACs for indications like unusual-site thromboses like cerebral venous thrombosis and non-cirrhotic portal vein thrombosis, where DOACs have been trialled but not yet been accepted for widespread use.^{1,2} Another area, where this is similarly relevant is patients who have an underlying malignancy who may be receiving chemotherapy or their treatment may have been withheld due to the pandemic from concerns of immunosuppression. Although, low molecular weight heparin (LMWH) is the drug of choice in patients with cancer, recent trials have clearly shown equal efficacy for DOACs and LMWH in these patients and appropriate patients (except those with gastrointestinal and genitourinary cancers) may be considered for DOACs treatment of cancer-associated thrombosis.^{3,4,5,6} DOAC are certainly of more practical use than VKA especially during COVID-19 pandemic, as they do not need laboratory monitoring. In addition, they proved safer than VKA in terms of incidence of intracranial bleeding, although it must be emphasized, contrary to what Hermans and Lambert implied in their letter, that they did not prove safer than VKA in terms of incidence of bleeding in other sites (especially gastrointestinal), which may be severe enough to require transfusion of blood products. We do, however, advice caution (not avoidance) with DOACs in patients admitted with COVID-19 illness (who can continue to take oral medications) for the following reasons

- Interactions with anti-retroviral drugs should be taken into account since some of these drugs have been considered in the treatment of COVID-19 pneumonia. We usually check with <https://www.hiv-druginteractions.org/> to ensure co-prescription is safe
- Those who may have unstable kidney function need to be closely monitored when they develop critical illness due to the renal excretion of DOACs and likelihood of accumulation

The authors also highlight the importance of extended half-life haemophilia products (EHL) and emicizumab in the management of patients with haemophilia in the COVID-19 pandemic era. Once again, this approach is very advantageous and in keeping with the international guidance of 'social distancing' wherein patients do not have to attend hospitals and can have the protection of higher trough factor levels (with EHLs) and possibly less bleeding than the conventional therapies.

Once the efforts of the self-less medical community all around the world get on top of the pandemic soon, it is important that we retrospectively analyse the lessons learned from our change of practice in these extenuating circumstances and use them to benefit the thrombosis and haemostasis community in the future.

References

1. Lurkin A, Derex L, Fambrini A, Bertoletti L, Epinat M, Mismetti P, Dargaud Y. Direct Oral Anticoagulants for the Treatment of Cerebral Venous Thrombosis. *Cerebrovasc Dis*. 2019;48(1-2):32-37
2. Naymagon L, Tremblay D, Zubizarreta N, Moshier E, Troy K, Schiano T, Mascarenhas J. The efficacy and safety of direct oral anticoagulants in noncirrhotic portal vein thrombosis. *Blood Adv*. 2020 Feb 25;4(4):655-666.
3. Key NS, Khorana AA, Kuderer NM, Bohlke K, Lee AYY, Arcelus JI, et al. Venous Thromboembolism Prophylaxis and Treatment in Patients With Cancer: ASCO Clinical Practice Guideline Update. *J Clin Oncol*. 2020 Feb 10;38(5):496-520.
4. Raskob GE, van Es N, Verhamme P et al. Edoxaban for the treatment of cancer-associated venous thromboembolism. *N Engl J Med* 2018; 378(7):615–624.47.
5. Young AM, Marshall A, Thirlwall J et al. Comparison of an oral factor Xa inhibitor with low molecular weight heparin in patients with cancer with venous thromboembolism: results of a randomized trial (SELECT-D). *JCO* 2018; 36(20): 2017–2023.48.
6. Agnelli G, Becattini C, Meyer G, Muñoz A, Huisman MV, Connors JM, et al; Caravaggio Investigators. Apixaban for the Treatment of Venous Thromboembolism Associated with Cancer. *N Engl J Med*. 2020 Mar 29. doi: 10.1056/NEJMoa1915103.